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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,141	02/15/2002	Gerhard Hartwich	PATKRI P03AUS	7623

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EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/069,141	Hartwich
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 15, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *58-72 and 75-86* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *58-72 and 75-86* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Status of the Application

1. The amendment received on July 15, 2003 has been entered. Claims 58 and 60 have been newly amended and claims 73 and 74 have been canceled without prejudice towards further prosecution. Claims 58-72 and 75-86 are pending and under consideration.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth In this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth In section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill In the art to which said subject matter pertains. Patentability shall not be negatived by the manner In which the invention was made.

3. Claims 58-72, and 75-86 are rejected under 35 U.S.C. 103(a) over Barton et al. (U.S. Patent 6,221,586 B1) (April 24, 2001) In view of Lee et al. (U.S. Patent 4,749,653) (June 7, 1988).

Barton et al teaches a nucleic acid oligomer modified by attaching a catalytically redox-active moiety, characterized In that the catalytically redox-active moiety is selected from

redox proteins and enzymes which use prosthetic groups such as flavins or NAD (Abstract, Column 5, lines 6-44, and Column 11, lines 5-11 and Column 11, line 63 to Column 14, line 36).

Barton et al teaches a nucleic acid oligomer, wherein the catalytically redox-active moiety is covalently attached to the phosphoric-acid , carboxylic-acid, or amine groups or to a sugar of the nucleic acid oligomer backbone (Claim 3 and Column 13, lines 2-6 and Figure 1).

Barton et al teaches a nucleic acid oligomer, wherein the modified nucleic acid oligomer sequence-specifically binds single stranded DNA (Column 12, lines 30-36).

Barton et al teaches a nucleic acid oligomer, wherein the modified nucleic acid oligomer is a DNA oligomer (Examples 1-14).

Barton et al teaches a nucleic acid oligomer, wherein following attachment to the nucleic acid oligomer, the catalytically redox-active moiety possesses electrocatalytic activity (Column 12, lines 55-65).

Barton et al teaches a nucleic acid oligomer, wherein multiple catalytically redox-active moieties are attached to the nucleic acid oligomer (Figure 1).

Barton et al teaches a method of producing a modified nucleic acid oligomer, wherein, alternatively, the nucleic acid oligomer is bound to the catalytically redox-active moiety by one or more amidations with amine groups of the catalytically redox-active moiety or by thioester formation with thioalcohol groups of the catalytically redox-active moiety (Examples 1 and 3).

Barton et al teaches a method of producing a modified nucleic acid oligomer, wherein one or more branched or linear molecular moieties of any composition and chain length

are covalently attached to the catalytically redox-active moiety and the branched or linear molecule moieties possess, alternatively, a reactive amine, hydroxyl, thiol, acid or aldehyde group for covalent attachment to a nucleic acid oligomer (Examples 1 and 3 and claims 3 and 7 and Figure 1).

Barton et al. teaches a method of producing a modified nucleic acid oligomer, wherein the shortest continuous link between the nucleic acid oligomer and the catalytically redox-active moiety is a branched or linear molecular moiety having a chain length of 1-20 atoms (Column 8, lines 16-19 and Figure 1).

Barton et al. teaches a modified conductive surface, wherein one or more types of modified nucleic acid oligomers are attached to a conductive surface (Figure 1 and Examples 1 and 3).

Barton et al. teaches a modified conductive surface, wherein the surface consists of a metal or semiconductor (Examples 1-14).

Barton et al. teaches a modified conductive surface, wherein the attachment of the modified nucleic acid oligomers to the conductive surface occurs covalently by chemisorption or physisorption of the phosphoric-acid , carboxylic-acid, or amine groups or to a sugar of the nucleic acid oligomer backbone (Examples 1 and 3 and Column 13, lines 35-56).

Barton et al. teaches a modified conductive surface, wherein alternatively, a reactive amine, hydroxyl, thiol, acid or aldehyde group is attached covalently or by chemisorption or physisorption to the conductive surface (Examples 1 and 3 and claims 3 and 7 and Figure 1).

Barton et al. teaches a modified conductive surface, wherein only one type of modified nucleic acid oligomer each is attached In a spatially delimited area of the conductive surface (Figures 1 and 6 and Example 11).

Barton et al. teaches a method of producing a modified conductive surface, wherein one or more types of modified nucleic acid oligomers are applied to a conductive surface and thereafter, a modification of the nucleic acid oligomers is carried out (Examples 1-14).

Barton et al. teaches a method of producing a modified conductive surface, wherein the nucleic acid oligomers are hybridized with the respective complementary nucleic acid oligomer strand and applied to the conductive surface In the form of the double-strand hybrid (Figures 1, and 5-7 and Examples 4-10).

Barton et al. teaches a method of producing a modified conductive surface, wherein the nucleic acid oligomers are applied to the conductive surface In the presence of further chemical compounds that are likewise attached to the conductive surface (Examples 1-6).

Barton et al. teaches a method of electrochemically detecting oligomer hybridization events, wherein one or more modified conductive surfaces are brought into contact with nucleic acid oligomers and, subsequently, detection of the electrical communication between the catalytically redox-active moiety and the respective conductive surface takes place (Examples Figure 5 and Examples 2, 5-8, 10-14).

Barton et al. teaches a method, wherein detection takes place by cyclic voltammetry, amperometry, potentiometry, or conductivity measurement (Example 4 and Column 8, lines 21-29).

Barton et al. teaches a method of producing a modified conductive surface, wherein electrochemical detection is initiated by adding the substrate to the catalytically redox-active moiety attached to the conductive surface via a nucleic acid oligomer (Example 4 and Column 12, lines 21-65).

Barton et al. teaches a method of producing a modified conductive surface, wherein the addition of the substrate to the catalytically redox-active moiety attached to the conductive surface via a nucleic acid oligomer is limited to an area of the conductive surface having one or more modified nucleic acid oligomer types (Example Examples 4 and 11).

Barton et al. does not teach a catalytic redox-active moiety selected from alcohol dehydrogenase, lactate dehydrogenase, and peroxidase.

Lee et al. teaches a catalytic redox-active moiety selected from alcohol dehydrogenase, lactate dehydrogenase, and peroxidase (which inherently use prosthetic groups flavins or NAD) (Column 4, line 45 to column 5, line 7).

It would have been *prima facie* obvious to one having ordinary skill In the art at the time the invention was made to substitute and combine a structurally and functionally equivalent catalytic redox-active moiety selected from redox enzymes alcohol dehydrogenase, lactate dehydrogenase, and peroxidase of Lee et al. In the modified nucleic acid oligomer of Barton et al. since Lee et al. states, "A variety of enzymes are suitable In the present invention, especially those which contain a group capable of reacting with the cross-linking agent. For example, useful enzymes may have an amino group which is capable of reacting with an aldehyde or an isocyanate so as to be cross-linked with itself and/or the polymer (Column 4, lines 45-50) ".

Moreover, further motivation is provided by Barton et al as Barton et al states, "The present invention provides a highly sensitive and accurate method based on an electrochemical assay using intercalative, redox-active species to determine the presence and location of a single or multiple base-pair mismatches (Column 11, lines 12-15)". An ordinary practitioner would have been motivated to substitute and combine a catalytic redox-active moiety selected from alcohol dehydrogenase, lactate dehydrogenase, and peroxidase of Lee et al. In the modified nucleic acid oligomer of Barton et al. In order to achieve the express advantages, as noted by Lee et al., of useful enzymes capable of reacting with an aldehyde or an isocyanate so as to be cross-linked with itself and/or the polymer and also In order to achieve the express advantages, as noted by Barton et al., of an invention which provides a highly sensitive and accurate method based on an electrochemical assay using intercalative, redox-active species to determine the presence and location of a single or multiple base-pair mismatches.

Response to Amendment

4. In response to amendment, 112 (first and second paragraph) rejections have been withdrawn. However, 103 (a) rejection has been maintained properly.

Response to Arguments

5. Applicant's arguments filed on July 15, 2003 have been fully considered but they are not persuasive.

In response to applicant's argument (page 8, line 1 to page 9, line 8 and page 10, last paragraph) that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., (A) the absence of an intercalator, (B) a catalytically redox-active moiety not having a flat or even shape and c) the exact structure of the modified nucleic acid oligomers must be known) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant also argues (Page 9, third paragraph) that one of the combinatory references (Lee et al) teaches alcohol dehydrogenase of the claimed invention but does not teach the attachment of this enzyme to oligonucleotide. This argument is not persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It was clearly mentioned in the last office action that Barton et al teaches the attachment of redox-active moieties to oligonucleotide (Examples 1 and 3).

Applicant also argues (Page 10, second paragraph, to third paragraph) that Lee et al has a motivation to determine the activity of the immobilized enzyme, whereas the instant claims has the motivation to detect sequence-specific nucleic acid oligomer hybridization events. This argument is not persuasive. In response to applicant's argument that the cited reference of

Lee et al has another reason or motivation to form the same structure of the claimed invention, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Moreover, applicant argues (Page 10, second and third paragraph) that Lee et al uses the enzymes linked to polymers to determine the activity of the immobilized enzyme, whereas the instant invention uses the same to detect sequence-specific nucleic acid oligomer hybridization events. This argument is not persuasive.In response to applicant's argument that 103(a) rejection should be withdrawn because the intended use of the claimed invention is different from the cited prior art, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

In view of the response to argument, previous 103(a) rejection is hereby maintained properly.

Conclusion

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703)605-1237.

Arun Chakrabarti,

Patent Examiner,

July 28, 2003

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